CALGB-49907: Adjuvant Chemotherapy in Elderly Women

Relatively few randomized trials of adjuvant chemotherapy have included substantial numbers of elderly women, so a relative paucity of research data exists with regard to the risks and benefits of this intervention. This is particularly problematic in older women with estrogen receptor-negative tumors who will not receive endocrine therapy. Another common clinical dilemma is the elderly woman with an estrogen receptor-positive tumor for whom the incremental benefits and risks of chemotherapy in addition to endocrine treatment must be considered. An important related trial is being led by Dr Hyman Muss. CALGB-49907 randomly assigns elderly women with primary breast cancer to either the orally administered fluoropyrimidine prodrug capecitabine, or AC or CMF chemotherapy. In addition to evaluating disease-free and overall survival, a number of key quality-of-life endpoints are being evaluated.

**CALGB-49907: ADJUVANT CMF OR AC VERSUS BREAST CANCER PATIENTS IN 65 YEARS AND OLDER**

**Table: Summary of Efficacy**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Response Rate</th>
<th>Complete Response</th>
<th>Median Time to Disease Progression</th>
<th>Median Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine</td>
<td>30% (25-40)</td>
<td>3%</td>
<td>4.1 months</td>
<td>11.6 months</td>
</tr>
<tr>
<td>CMF</td>
<td>26% (19-35)</td>
<td>0%</td>
<td>4.3 months</td>
<td>12.2 months</td>
</tr>
</tbody>
</table>

**Randomization:**

- 1:1 randomization to Capecitabine or CMF

**Stratification:**

- Age (65-69, 70-74, >74, 80+)
- Menopausal status: ovarian failure or amenorrhea
- Number of positive lymph nodes
- Number of positive axillary nodes
- Type of surgery

**Carcinomas versus fluoropyrimidine/antimetabolites (CMF) as first-line therapy (n=90)**

<table>
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<tr>
<th>Treatment</th>
<th>Complete Response</th>
<th>Median Time to Disease Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine</td>
<td>12% (7-19)</td>
<td>4.1 months</td>
</tr>
<tr>
<td>CMF</td>
<td>0%</td>
<td>4.3 months</td>
</tr>
</tbody>
</table>

**Source:** NCI Physician Data Query, October 2004

**In addition to the more familiar ER, PR and HER2 markers, we are looking at some interesting predictive and prognostic markers and other biological markers. We are also examining how these drugs are metabolized in the elderly population. The data from the metastatic setting provided the rationale for selecting capecitabine for this trial. In addition to the convenience of an oral regimen, the trials comparing capecitabine to single-agent paclitaxel and to CMF demonstrated benefits from capecitabine in time to progression. However, capecitabine is not a benign drug, so we are closely monitoring patients.**

— Maria Theodoulou, MD

**Capecitabine in Elderly Patients**

We did a small, randomized Phase II trial comparing intravenous CMF and full dose capecitabine as front-line therapy in elderly patients aged 55 years or older in the metastatic setting. The response rate with capecitabine was 30 percent compared to 16 percent with intravenous CMF.

In a randomized Phase II trial of patients pretreated with an anthracycline, comparing paclitaxel every three weeks to capecitabine, the response with capecitabine was 36 percent compared to 26 percent with paclitaxel. The confidence intervals were widely overlapping, so we couldn’t conclude that capecitabine is superior.

What can we say from these two studies is that it’s certainly unlikely that capecitabine is worse than CMF or paclitaxel. It’s interesting how quickly capecitabine has moved to trials in the adjuvant setting. In women over age 65, the role of chemotherapy is unknown. For women over 70, in particular, the overview analysis includes so few patients in that age group that I think it’s very reasonable to compare capecitabine to AC or CMF.

— Joyce O’Shaughnessy, MD

**CALGB-49907: QUALITY-OF-LIFE SUBPROTOCOL**

Capecitabine is an obvious choice to study in the adjuvant setting. I’m most interested in Hyman Muss’ Intergroup study comparing capecitabine versus AC or CMF in women over age 65. Based on the chemistry of capecitabine, it wouldn’t surprise me if it proves to be equivalent in efficacy with a superior toxicity profile. In addition, it has the advantage of being an oral regimen. US Oncology and MD Anderson each have adjuvant studies evaluating the combination of capecitabine and docetaxel, but these trials are not mature and it will be some time before we know the results.

— Daniel J Rudman, MD